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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,540	03/08/2001	Adrian Bot	A30571-A-PCT/USA-A	7183

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BAKER BOTTS L.L.P.
44TH FLOOR
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-4498

EXAMINER	
SGAGIAS, MAGDALENE K	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/801,540	BOT ET AL.	
	Examiner	Art Unit	
	Magdalene K. Sgagias	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 10/31/06 have been fully considered but they are not persuasive. The amendments have been entered. Claims 1-2 are pending and under consideration. Claim 3 is cancelled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 rejection under 35 U.S.C. 102(b) as being anticipated by Ali et al. (Infect Immun, 38(2): 610-19, 1982) is maintained.

Claims 1 and 2 rejection under 35 U.S.C. 102(b) as being anticipated by Murphy et al. (J Clin Microbiol 24(2): 197-202, 1986) is maintained.

Applicants argue that in both references of Ali et al, and Murphy et al, different forms of viruses were used. Applicants argue, in Ali live attenuated viruses were administered and in Muprhy inactivated vaccines were administered, while the present invention focuses on the use of naked recombinant nucleic acid vaccines. These arguments are not persuasive because in both cases a reasonable interpretation of the breadth of the claims would include the administration of an attenuated virus, which contains the nucleic acid that encodes the relevant epitopes, which provides the basis of immunization of the infant mammal.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 rejection under 35 U.S.C. 103(a) as being unpatentable over Ricigliano et al, (US Patent 5,795,872) and Milagres et al, (Infect Immun, 62(10): 4419-24, 1994) is maintained.

Claims 1 and 2 rejection under 35 USC 103(a) as being unpatentable over **Fynan et al,** (Proc Natn Acad Sci, 90(24): 11478-82, 1993) and **Milagres et al,** (Infect Immun, 62(10): 4419-24, 1994) is maintained.

Claims 1 and 2 are rejected under 35 USC 103(a) as being unpatentable over **Ricigliano et al,** (US Patent 5,795,872) and **Milagres et al,** (Infect Immun, 62(10): 4419-24, 1994).

The elected invention is drawn to immunizing an infant mammal against a target antigen comprising inoculating the infant mammal with an effective amount of a naked nucleic acid encoding a relevant epitope of the target antigen in a pharmaceutically effective carrier such that the relevant epitope is expressed in the infant mammal and induces a cytotoxic T cell response against a pathogen in an infant mammal. At the time of filing DNA constructs and use of said constructs to express an antigen as a vaccine were known. Ricigliano et al, teach a specific DNA construct for use in immunization (see allowed claims). Ricigliano et al, teach that nucleotide sequence of any antigen can be inserted into the construct, and provide methods where the DNA is delivered to the muscle resulting in expression and immune response.

Ricigliano et al, teach a variety of specific known antigens (claim 2 for example), however, fail to specifically teach to immunize with antigens to *Neisseria meningitiditis* nor specifically the immunization of infants. At the time of filing Milagres et al, teach the outer membrane protein of *Neisseria meningitiditis* serves an appropriate and effective vaccine antigen in vaccinating infants from 3 to 83 months of age (see summary abstract). At the time of filing immunization of infants for *Neisseria meningitiditis* with subunit vaccines were known and practiced and the use of DNA vaccines provides a means to deliver such antigens to a subject. Therefore, it would have been *prima facia* obvious to one having ordinary skill in the art at the time the invention was made to use DNA constructs such as those provided in Ricigliano et al, for use as vaccine through the expression of protein antigens from *Neisseria meningitiditis*. One having ordinary skill in the art would have been motivated to substitute the use of DNA vectors over conventional protein vaccines because of the limitations of providing purified proteins and as a source of a more stable vaccine (i.e. DNA versus protein/attenuated virus). There would have been a reasonable expectation of success given the results of Milagres et al, for the immunization of infants to *Neisseria meningitiditis* with a DNA vector as taught in Ricigliano et al, expressing a specific antigen such as the outer membrane protein of *Neisseria meningitiditis* (Milagres et al,).

Thus, the claimed invention was prima facie obvious in the absence of evidence to the contrary.

Applicants argue that it would not have been obvious for one skilled in the art to substitute DNA vectors in place of the protein vaccines taught in the cited art. Applicants argue that Milagres discloses a study where protein vaccine was administered to children of various ages, grouped separately as 3-23 months, 24-47 months, and 48-83 months. Applicants also argue Milagres used three assays to measure the antigen/antibody levels of the child

populations including antigenic analysis (ELISA), bactericidal data, the functional immune responses were age dependent, that bacterial titers were significantly lower as were bactericidal antibodies in children less than 24 months as compared to the older children. Applicants further argue the remaining tests were deemed not reliable for various reasons. These arguments are not persuasive.

Milagres teaches a vaccine that is effective in children of various ages including infants within the age of birth to six months irrespective of the assay method for measurement of bacterial titers. Applicants have not provided reasoning as to why the remaining tests were deemed not reliable, however, despite whether the remaining tests were deemed not reliable did not exclude or obviated Milagres' conclusion that the bactericidal assay was a good laboratory-based functional assay for the study of vaccine immunogenicity and the functional immune responses were age dependent.

Applicants argue that the currently amended claims define the target population of infants within the age of birth to six months and further define the vaccine as a naked recombinant nucleic acid vaccine. Applicants argue Milagres conclusion that the functional immune responses are age dependent make it impossible to know what the results were for children under age of 3 months or what the breakdown of results were within each group of the study. There is no expectation here that the functional immune response was even present, let alone successful, in the claimed "infant" population. Applicants further argue Milagres' conclusions regarding the age dependent nature of the immune response would not create an expectation of success in an infant population as presently claimed. These arguments are not persuasive.

Milagres teaches an effective DNA vaccine against *Neisseria meningitiditis* and does not exclude a functional immune response. Milagres teaches that the postvaccination

seroconversion rate of children under 24 months of age was less than the naturally acquired levels of those over 24 months of age and the age specific incidence of group B meningococcal diseases disease is much higher in children under 1 year old which indicates a functional immune response and does not exclude children within the age of birth to six month of age as presently claimed. There would have been a reasonable expectation of success given the results of Milagres et al, for the immunization of infants to *Neisseria meningitiditis* with a DNA vector as taught in Ricigliano et al, expressing a specific antigen such as the outer membrane protein of *Neisseria meningitiditis* (Milagres et al,) especially since Milagres teaches that the outer membrane protein of *Neisseria meningitiditis* serves an appropriate and effective vaccine antigen in vaccinating infants from 3 to 83 months of age (see summary and abstract).

Applicants argue Milagres administered a protein vaccine to conduct his studies, in contrast, the presently claimed invention relates to the administration of naked recombinant nucleic acids encoding a relevant epitope of a target antigen. Applicants argue reliance on Ricigliano fails to provide one skilled in the art the presently claimed invention. Applicants argue Ricigliano is broadly directed to DNA constructs useful for immunization comprising muscle specific regulatory elements and a DNA sequence. Applicants argue that Ricigliano is not enabling for any "antigen" rather Ricigliano requires that the DNA construct contains a muscle specific regulatory element of muscle isozyme of creatine kinase with a specific nucleotide sequence (SEQ ID NO:1; see claim 1). Applicants further argue

One of ordinary skill in the art at the time of filing could easily have substituted the use of DNA vectors over conventional protein vaccines because of the limitations of providing purified proteins and as a source of a more stable vaccine. Applicants have provided no evidence as to why the Ricigiano DNA constructs comprising muscle specific regulatory elements and a DNA sequence, which are recombinant nucleic acid constructs (DNA) and which are useful for both

immunization or gene therapy is not obvious. Any construct containing any antigen is naked recombinant nucleic acid. Any nucleotide sequences inserted into the construct would correspond to naked recombinant nucleic acid stated in the claims merely because they are nucleic acids. The language in the claims does not in any manner limit the claims to a nucleic acid encoding a pathogen epitope.

Claims 1 and 2 are rejected under 35 USC 103(a) as being unpatentable over **Fynan et al,** (Proc Natn Acad Sci, 90(24): 11478-82, 1993) and **Milagres et al,** (Infect Immun, 62(10): 4419-24, 1994).

As noted above, at the time of filing DNA constructs and use of said constructs to express an antigen as a vaccine were known. **Fynan et al,** teach a specific DNA construct for use in immunization (see allowed calims). **Fynan et al,** teach that nucleotide sequence of any antigen can be inserted into the construct, and provide methods where the DNA is delivered to the muscle resulting in expression and an immune response. **Fynan et al,** teach a variety of specific known antigens and different routes of administration, however, fail to specifically teach to immunize with antigens to *Neisseria meningitiditis* nor specifically the immunization of infants. At the time of filing immunization of infants for *Neisseria meningitiditis* with subunit vaccines were known and practiced and the use of DNA vaccines provides a means to deliver such antigens to a subject. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to use DNA constructs such as those provided in Ricigliano et al, for use as vaccine through the expression of protein antigens from *Neisseria meningitiditis*. One having ordinary skill in the art would have been motivated to substitute the use of DNA vectors over conventional protein vaccines because of the limitations of providing purified proteins and as a source of a more stable vaccine (i.e. DNA versus protein/attenuated virus). There would have been a reasonable expectation of success given the results of

Milagres et al, for the immunization of infants to *Neisseria meningitiditis* with a DNA vector as taught in Ricigliano et al, expressing a specific antigen such as the outer membrane protein of *Neisseria meningitiditis* (Milagres et al,).

Thus, the claimed invention was prima facie obvious in the absence of evidence to the contrary.

The prior art made of record and nor relied upon is considered pertient to applicant's disclosure.

Oduntan et al, Ann Trop Med Parasitol, 72(2): 111-5, 1978, The immunological response of Nigeria infants to attenuated and inactivated polio vaccines, provides further evidence that infants have been vaccinated with other types of attenuated viruses.

Montgomery et al, Cur Opin Biotechnol, 5(5): 505-10, 1994; Protein expression in vivo by injection of polynucleotides, provides further evidence that the principle of DNA vaccines, expression of a protein upon injection of a polynucleotide were known at the time of filing.

Lagging et al, J Vir, 69(9): 5859-5863, 1995, provides evidence that expression if antigens result in an immune response in an individual, and may serve as the basis of a vaccine.

Applicants argue that, Fynan teaches a variety of specific known antigens for use in DNA constructs for immunization and the Examiner concedes that Fynan fails to teach immunization to a specific antigen or the immunization of infants. These arguments are not persuasive.

Applicants have not provided evidence why Fynan is not enabling. The use of DNA vaccines can be used with various modes of gene delivery methods. The language in the claims does not in any manner limit the claims to a nucleic acid encoding a pathogen epitope. At the

time of filing immunization of infants for *Neisseria meningitiditis* with subunit vaccines were known and practiced and the use of DNA vaccines provides a means to deliver such antigens to a subject including infants within the age of birth to six months. One having ordinary skill in the art would have been motivated to substitute the use of DNA vectors over conventional protein vaccines because of the limitations of providing purified proteins and as a source of a more stable vaccine (i.e. DNA versus protein/attenuated virus).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1 and 2 rejection under 35 U.S.C. 101 as claiming the same invention as that of claims 1-47 of copending Application No. 10/351,630 is maintained for reasons provided in the office action mailed 10.31.06.

Applicants argue that in the event the claims are allowed in either case, appropriate claim cancellations or amendments will be made in the co-pending application to ensure that they are not coextensive in scope. Since Applicant has not provided such amendment said rejection is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias, Ph.D.
Art Unit 1632

PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600